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1	BRS	L1	4	aerothericin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/30 12:47			0
2	BRS	L2	967	mycoses	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/30 12:47			0
3	BRS	L3	1	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/30 12:48			0

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=> s aerothricin  
L1 11 AEROTHRICIN

=> duplicate remove l1  
DUPLICATE PREFERENCE IS 'CAPLUS, EMBASE, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L1  
L2 7 DUPLICATE REMOVE L1 (4 DUPLICATES REMOVED)

=> d l2 1-7 ibib abs

L2 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
ACCESSION NUMBER: 2002:136646 CAPLUS  
TITLE: \*\*\*Aerothricins\*\*\* : a new class of .beta.-glucan inhibitors  
AUTHOR(S): Anon.  
SOURCE: Expert Opinion on Therapeutic Patents (2002), 12(2), 315-318  
CODEN: EOTPEG; ISSN: 1354-3776  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; Miscellaneous  
LANGUAGE: English  
AB Two patent applications assigned to Basilea Pharmaceutica describe \*\*\*aerothricin\*\*\* natural product mols. and a large series of semi-synthetic mols. claimed as antifungal drugs that inhibit the .beta.-1,3-D-glucan component of the cell wall. The semi-synthetic mols., considerably larger than the previous hexapeptide echinocandin and pneumocandin mols., contain various basic amino acids and a large series of aminoalkyl groups and are presumably more water-sol. than the natural product \*\*\*aerothricins\*\*\*. Overall, the antifungal in vitro susceptibility results compared favorably with other .beta.-glucan inhibitors. Results are also presented for select compds. in mouse models of mycoses that indicate good activity. One of the applications is largely focused on formulations of pharmacol.-active cyclic peptides with absorption enhancers delivered by the intranasal route and provides pharmacokinetic data in cynomolgous monkeys in support of the claims.  
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:545715 CAPLUS  
DOCUMENT NUMBER: 135:137714  
TITLE: Preparation of \*\*\*aerothricins\*\*\*, novel cyclic compounds having antifungal activity  
INVENTOR(S): Kohchi, Masami; Masubuchi, Kazunao; Murata, Takeshi; Okada, Takehiro; Shimma, Nobuo

PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.  
 SOURCE: PCT Int. Appl., 44 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053322	A2	20010726	WO 2001-EP251	20010111
WO 2001053322	A3	20020131		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001025148	A5	20010731	AU 2001-25148	20010111
US 2001031728	A1	20011018	US 2001-760949	20010116

PRIORITY APPLN. INFO.: EP 2000-100807 A 20000117  
 WO 2001-EP251 W 20010111

OTHER SOURCE(S): MARPAT 135:137714  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB \*\*\*Aerothricin\*\*\* derivs. I [R1 = N-(3-aminopropyl)-N-[(2S)-2,5-diaminovaleryl]amino, N-(3-aminopropyl)-N-[5-amino-2-[N,N-bis(2-aminoethyl)amino]valeryl]amino, N-(3-aminopropyl)-N-[5-amino-2-[N-(3-aminopropyl)amino]valeryl]amino, N-(2-aminoethyl)-N-[5-amino-2-[N,N-bis(2-aminoethyl)amino]valeryl]amino or ornithylornithylamino; R2 = H, Me; R3 = H, OH] or pharmaceutically acceptable salts were prepd. for use as fungicides. Thus, \*\*\*aerothricin\*\*\* 3 (I; R1 = NH2, R2 = R3 = H), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions, was treated with acrylonitrile in MeOH in the presence of Et3N to give \*\*\*aerothricin\*\*\* 120 (I; R1 = NHCH2CH2CN, R2 = R3 = H). Coupling of \*\*\*aerothricin\*\*\* 120 with Boc-L-Orn(Boc)-OH (Boc = tert-butoxycarbonyl, Fmoc = 9-fluorenylmethoxycarbonyl) in DMF using BOP reagent, HOBT hydrate and N-ethyldiisopropylamine, followed by deprotection with TFA and hydrogenolysis over 10% Pd on charcoal, afforded \*\*\*aerothricin\*\*\* 132 [I; R1 = L-Orn-N[(CH2)3NH2], R2 = R3 = H]. The \*\*\*aerothricins\*\*\* of formula I exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized \*\*\*aerothricins\*\*\* are much less cytotoxic to hepatocytes than the known cyclic peptide derivs. WF11243 and LY303366.

L2 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:545525 CAPLUS  
 DOCUMENT NUMBER: 135:157672  
 TITLE: Cyclic peptide compositions for nasal administration  
 INVENTOR(S): Horii, Ikuro; Kobayashi, Kazuko; Shimma, Nobuo; Yanagawa, Akira  
 PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.  
 SOURCE: PCT Int. Appl., 117 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052894	A2	20010726	WO 2001-EP163	20010109
WO 2001052894	A3	20020131		

W: AE, AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,  
 DE, DK, EE, ES, FI, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,  
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,  
 MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
 TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,  
 MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001038824 A1 20011108 US 2001-765846 20010119

PRIORITY APPLN. INFO.: EP 2000-101057 A 20000120

OTHER SOURCE(S): MARPAT 135:157672

AB The present invention relates to a nasal compn. of physiol. active cyclic peptides and salts that are prepd. by homogeneously dispersing an active cyclic peptide such as antifungal cyclic peptides ( \*\*\*aerothricin\*\*\* , echinocandin analogs, pneumocandin analogs, and aureobasidin), antibacterial cyclic peptides (e.g., vancomycin, daptomycin), cyclosporin A, lanreotide, vapreotide, vasopressin antagonist and eptifibatide in a unique carrier. The powdery or cryst. carrier contains a water insol. polyvalent metal carrier, or org. carrier having a mean particle size of 20-500 .mu.m, in the presence or absence of an absorption enhancer and by homogeneously adsorbing onto the carrier, and its use for therapeutic treatment of disease such as systemic fungal infections by intranasal administration. The compn. can be nasally administered in a powder form. Thus, 201 mg \*\*\*Aerothricin\*\*\* 133 and 599 mg CaCO3 (mean particle size: 40-60 .mu.m) were mixed well. Then, 200 .mu.L water was added, and mixing was continued until the mixt. became a paste and the resulting pasty solid was freeze-dried at -50.degree., and further dried at 300.degree. for 3 h in vacuo. After large particles in the dry powder were broken into small particles, 8 mg of calcium stearate was added and the mixt. was passed through 180-.mu.m-mesh. \*\*\*Aerothricin\*\*\* 133 was synthesized by a series of steps.

L2 ANSWER 4 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001259444 EMBASE

TITLE: Synthesis and biological activity of novel macrocyclic antifungals: Modification of the tyrosine moiety of the lipopeptidolactone FR901469.

AUTHOR: Barrett D.; Tanaka A.; Harada K.; Watabe E.; Maki K.; Ikeda F.

CORPORATE SOURCE: D. Barrett, Medicinal Chemistry Research Lab., Fujisawa Pharmaceutical Co. Ltd., 2-1-6 Kashima, Yodogawa-ku, Osaka 532-8514, Japan. david\_barrett@po.fujisawa.co.jp

SOURCE: Bioorganic and Medicinal Chemistry Letters, (23 Jul 2001) 11/14 (1843-1849).

Refs: 15

ISSN: 0960-894X CODEN: BMCLE8

PUBLISHER IDENT.: S 0960-894X(01)00317-1

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Pharmacology

037 Drug Literature Index

052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A series of tyrosine-modified derivatives of the macrocyclic lipopeptidolactone FR901469 have been prepared and evaluated for in vitro and in vivo antifungal activity and for hemolytic activity towards red blood cells. Compound 14 displayed significantly reduced hemolytic potential at 1 mg/mL and a comparable protective effect to FR901469 in a mouse candidiasis model. .COPYRGT. 2001 Elsevier Science Ltd. All rights reserved.

L2 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER: 2001:800659 CAPLUS

DOCUMENT NUMBER: 136:95458

TITLE: Cell wall active antifungal agents

AUTHOR(S): Schwartz, Robert E.

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065-0900, USA

SOURCE: Expert Opinion on Therapeutic Patents (2001), 11(11), 1761-1772

PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. The recent American approval of Cancidas, a semi-synthetic echinocandin, for salvage treatment of aspergillosis has demonstrated that the cell wall is a clin. viable target for treating fungal infections. Recently, a variety of new, sulfated members of the echinocandin lipopeptide family have been reported, which, like other echinocandins, are glucan synthesis inhibitors. In addn., two new classes of lipopeptide glucan synthesis inhibitors, the \*\*\*aerothricin\*\*\* lipopeptidolactones and the Sankyo lipopeptides, have been identified, as well as a novel member of the papulacandin family of liposaccharide glucan synthesis inhibitors. The first new structural class of glucan synthesis inhibitors discovered in over 20 yr, the so-called sterol glycosides, is reviewed. Five different structural types within this class have been characterized. Finally, several novel compds. with cell wall antifungal activity based on inhibition of chitin synthase are reviewed.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001050795 EMBASE

TITLE: Update on antifungals targeted to the cell wall: Focus on .beta.-1,3-glucan synthase inhibitors.

AUTHOR: Georgopapadakou N.H.

CORPORATE SOURCE: N.H. Georgopapadakou, Antimicrobial Research, DuPont Pharmaceuticals, Experimental Station P.O. Box 80400, Wilmington, DE 19880-0400, United States. nafsikag@aol.com

SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/2 (269-280).  
Refs: 121

ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Currently available antifungal drugs for serious infections are either fungistatic and vulnerable to resistance (azoles) or fungicidal but toxic to the host (polyenes). Cell wall-acting antifungals are inherently selective and fungicidal, features that make them particularly attractive for clinical development. Three classes of such compounds, targeted respectively to chitin synthase (nikkomycins), .beta.-1,3-glucan synthase (echinocandins) and mannoproteins (pradimicins/benanomicins) have entered clinical development. While nikkomycins and pradimicins/benanomicins are no longer in development, echinocandins have emerged as potentially clinically useful and three compounds, caspofungin (MK-991, L-743,872), micafungin (FK-463) and anidulafungin (LY-303366) are in late clinical development (Phase II and III).

L2 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:84834 CAPLUS

DOCUMENT NUMBER: 132:137733

TITLE: Preparation of new antifungal agents, cyclic \*\*\*aerothricin\*\*\* analogs, for treatment of infectious diseases caused by pathogenic microorganisms

INVENTOR(S): Aoki, Masahiro; Kohchi, Masami; Masubuchi, Kazunao; Mizuguchi, Eisaku; Murata, Takeshi; Ohkuma, Hiroaki; Okada, Takehiro; Sakaitani, Masahiro; Shimma, Nobuo; Watanabe, Takahide; Yanagisawa, Mieko; Yasuda, Yuri

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005251	A1	20000203	WO 1999-EP5235	19990722
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9951630	A1	20000214	AU 1999-51630	19990722
BR 9912367	A	20010502	BR 1999-12367	19990722
EP 1100816	A1	20010523	EP 1999-936588	19990722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			EP 1998-113744	A 19980723
			EP 1999-107637	A 19990416
			WO 1999-EP5235	W 19990722

OTHER SOURCE(S): MARPAT 132:137733  
GI

/ Structure 1 in file .gra /

AB Novel antifungal \*\*\*aerothricins\*\*\* I [R1 = guanidino, trialkylammonio, NR10R11, NR15COR14, NR15COCH(NR10R11)R13 (Q), NHCOCHR13NHCOCH(NH2)R13, N[(CH2)nQ]2, N[(CH2)nQ][COCH(NR10R11)R13], or NR15COR12, where n = 2-5, R10, R11 = H, heteroaryl or mono- or diaminoheteroaryl, alkyl optionally substituted with one or more amino groups, aminoalkyl, cyano, guanidino, nitrogen-contg. heterocycle(s) or Ph group(s) contg. an amino, amidino or guanidino group, R12 is tetrahydro-2-pyrrolyl optionally substituted at N by R10 and by an amino group, R13 is a residue from natural or unnatural amino acids, R14 is alkyl substituted with one or more amino, guanidino, nitrogen contg. heterocycle or Ph group contg. an amino, amidino, or guanidino group, and R15 = H or R14-like group; R2 = H, HOSO2, alkyl or alkenyl optionally substituted with acyl, carbamoyl, amino, mono- or dialkylamino; R3 = H, OH, NO2, NH2, acylamino, (alkylcarbamoyl)amino, carboxyl, alkoxy, alkoxy carbonyl, (un)substituted alkyl, alkenyl, or alkynyl; R4 = alkyl, alkenyl, alkoxy or alkenyloxy optionally substituted with alkyl, aryl, cycloalkyl or F; R5 = CONH2, CN, CH2NH2; X is a single bond, aryl, biphenyl, terphenyl optionally contg. one or more heteroatom(s) and/or substituted with halo or alkyl; Y is a single bond, CH2, CH(alkyl), CONH, CON(alkyl); Z = O, NH, alkylamino; m = 0-4 (with provisos)] and pharmaceutically acceptable salts were prepd. Numerous processes for the prepn. of \*\*\*aerothricins\*\*\* of formula I are described. Thus, \*\*\*aerothricin\*\*\* 3 [I; R1 = NH2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me] (WF11243), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions in aq. medium, was treated with (2-oxoethyl)carbamic acid tert-Bu ester in MeOH in the presence of sodium cyanoborohydride and acetic acid to afford \*\*\*aerothricin\*\*\* 111 [I; R1 = N(CH2CH2NH2)2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me]. The \*\*\*aerothricins\*\*\* of formula I as well as pharmaceutically acceptable salts exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized \*\*\*aerothricins\*\*\* are less cytotoxic to hepatocytes than the known cyclic peptide derivs., e.g., WF11243.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s aerothricin/cn  
L3 0 AEROTHRICIN/CN

=> s aerothricin/ct  
'CT' IS NOT A VALID FIELD CODE  
L4 0 AEROTHRICIN/CT

=> logy  
LOGY IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> log y  
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FULL ESTIMATED COST 4.76 27.31

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